Chemistry & Biology

In This Issue

Everything You Need to Know about Chemical Lectinology

PAGE 983

Lectins are glycan-binding proteins involved in decoding the glycome and translating sugar code into specific functional outcomes. Belardi and Bertozzi review recent advances in chemical tools to study mammalian lectin biology in live cells and discuss the emerging view of lectin function that is highly sensitive to its organization

Activity-Based Probes for Bleomycin Hydrolase

PAGE 995

Bleomycin hydrolase is a neutral cysteine aminopeptidase that has been ascribed roles in many physiological and pathological processes, but its primary biological function remains enigmatic. van der Linden et al. describe the synthesis and evaluation of activity-based probes, irreversible inhibitors and fluorogenic substrates for bleomycin hydrolase.

Antibiotic Affects Both Host and Microbe to Deliver Double Punch

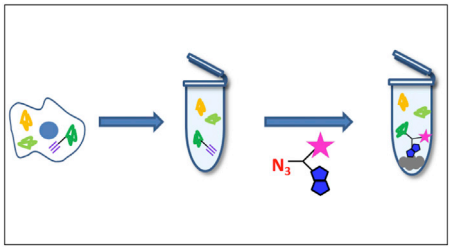
PAGE 1002

Zheng et al. discovered that thiostrepton-type thiopeptides exhibit a dual mode of action for anti-intracellular infection: in addition to directly targeting the ribosome of bacterial parasites, thiostrepton antibiotics induce autophagy to enhance host cell defense via activating endoplasmic reticulum stress pathways in eukaryotes.

Systems View of Protein Acylation during Infection

PAGE 1008

Serwa et al. develop a roadmap for the systematic investigation of protein acylation during infection, exemplified by analysis of a large complex DNA virus, herpes simplex virus. Using bioorthogonal probes and capture reagents, the authors quantify alterations to host acylation and identify novel virus-encoded acylated proteins.



Engineering Production of Primary Alcohols

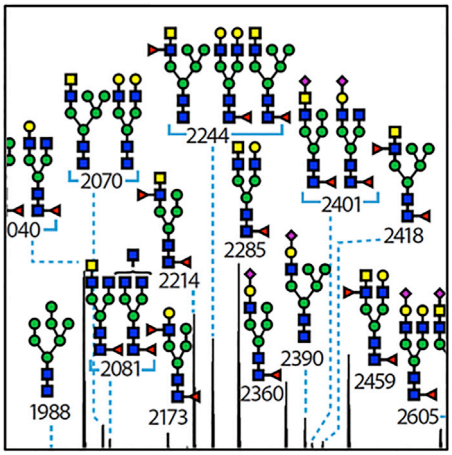
PAGE 1018

Barajas et al. report the structure of a unique termination domain employed in the reductive release of NRPS-generated natural products. The crystal structure, combined with computational and biochemical investigations, provides a comprehensive understanding of key factors that govern catalysis in this class of termination domains.

Linking Epigenetics and Metabolism

PAGE 1030

Montgomery et al. describe the application of a chemoproteomic approach to identify metabolic inhibitors of KAT enzymes. The authors find that long fatty acyl-CoAs strongly antagonize KAT activity and fatty acyl-CoA precursors reduce histone acetylation in cells.



Letting Cancer Cells Eat Themselves

PAGE 1040

Wang et al. provide an insight into the mechanism of Akt2-related resistance to autophagy and demonstrate a new avenue to broaden the chemical compound THPN application with Akt inhibitor to treat many types of cancers by induction of autophagic cell death.

How Glycosylation Sequons Rule

PAGE 1052

Murray et al., using tandem N-glycoprotein repeats to eliminate intracellular processing effects, demonstrate that introducing an aromatic residue at *n-2* relative to a glycosylation sequon increases oligosaccharyltransferase N-glycosylation efficiency and suppresses Golgi glycan remodeling, affording more homogeneous N-glycans.

Allosteric Communication Channels in Nicotinic Acetylcholine Receptors

PAGE 1063

Marotta et al. utilized non-canonical amino acid mutagenesis to establish an unaltered agonist binding site in the presence of a positive allosteric modulator, PNU-120596. Mutational analysis also discovered a network of residues vital to functional allosteric communication.

Targeting Seminal Amyloid to Fight HIV Infection

PAGE 1074

Castellano et al. design three disruptive technologies to rapidly antagonize seminal amyloid and reduce its ability to promote HIV infection by repurposing Hsp104, an amyloid-remodeling nanomachine from yeast.

Cyclotide Enters Cells via Phospholipids

PAGE 1087

Cyclotides are ultrastable cyclic peptides with potential to modulate intracellular targets. Henriques et al. show that they initiate cellular internalization via the targeting of specific phospholipids followed by both endocytosis and direct membrane translocation.

Learning More about *Mycobacterium tuberculosis*, One Structure at a Time

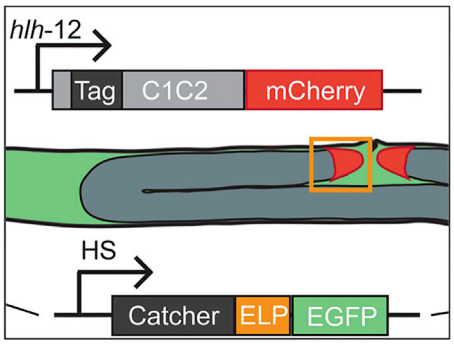
PAGE 1098

The structure of MmpL11-D2, determined by Chim et al., is reminiscent of RND transporters porter subdomains. MmpL3/11 D1 and D2 interact and D1-D2 heterodimeric models were built to present a first glimpse of MmpL periplasmic interdomain interactions.

Spy-ing on Worm Neurons

PAGE 1108

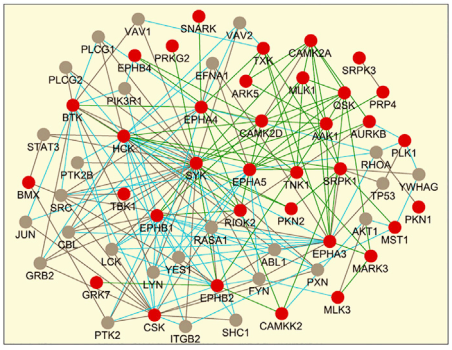
Bedbrook et al. describe a method for specifically labeling the membrane-localized fraction of channel rhodopsin expression using the genetically encoded, covalent binding SpyTag and SpyCatcher pair in live neurons and in vivo in *Caenorhabditis elegans*.



MMP Family Ties

PAGE 1122

Kukreja et al. presented the results of the high-throughput multiplexed profiling of the cleavage preferences of 18 proteinases from the main subgroups of the MMP family that lead to defining the substrate cleavage redundancy and specificity in the MMP family, to a better foundation for the follow-on structural-functional studies of MMPs, and to a means to predict in silico the cleavage targets of the individual MMPs.



Inserting Functional Proteins into Other Proteins

PAGE 1134

Peng et al. report a general approach, which is robust high-throughput screening based, for inserting functional proteins into proteins. The selected Leptin and single-chain FSH in human IgG were as potent as the native hormones.

Mapping the Kinase Addiction

PAGE 1144

Szwajda et al. developed a systems biology approach that integrates drug selectivity and sensitivity profiles to identify pharmacologically actionable signal addictions, both single and combinatorial, in given cancer cells. Such druggable molecular vulnerabilities may lead to stratified therapeutic strategies in various cancer subtypes.

